

phenylpiperidine. A depiction of the compound is provided on the attached sheet. Claims readable thereon are Nos. 1, 9, 19, 22, and 24-31".

"With respect to claims 27, 29 and 31, Applicant elects depression as clinical condition."

At present, claims 1, 9, 19-28 and 30 are under consideration and stand rejected. However, if the Examiner's Requirements have been correctly understood, claims 29 and 31 should also be entitled to consideration. Additionally, as indicated in Applicant's paper mailed July 19, 1999 (at page 1 thereof), none of claims 20, 21 or 23 should be presently under consideration as readable on the elected species. Only claims 1, 9, 19, 22, and 24-31 are readable thereon.

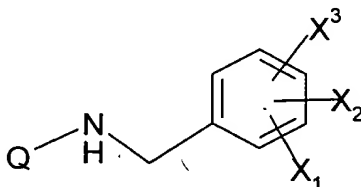
It is Applicant's intent to issue from the present application claims directed to method of treatment and pharmaceutical composition wherein the underlying compounds are those specifically covered by claims 1-24 of the immediate parent application, now U.S. Patent 5,773,450. It will thus be seen that the issues raised by the Examiner concerning prior art are readily addressed, such matters generally having dealt with in the file history of the parent application

Applicants amend as follows

Please cancel ~~all the~~ pending claims.

Please add the following new claims Nos 33-62

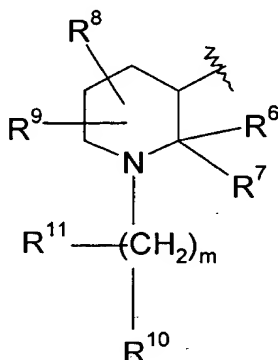
33. A pharmaceutical composition for treating or preventing a condition selected from the group consisting of inflammatory diseases, anxiety, colitis, depression or dysthymic disorders, psychosis, pain, gastroesophageal reflux disease, allergies, chronic obstructive airways disease, hypersensitivity disorders, vasospastic diseases, fibrosing and collagen diseases, reflex sympathetic dystrophy, addiction disorders, stress related somatic disorders, peripheral neuropathy, neuralgia, neuropathological disorders, disorders related to immune enhancement or suppression, and rheumatic diseases in a mammal, comprising an amount of a compound according to the following formula,



wherein X¹ is hydrogen (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms or (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms;

X^2 and X^3 are independently selected from halo, hydrogen, nitro, (C_1-C_{10}) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_{10}) alkoxy optionally substituted with from one to three fluorine atoms, trifluoromethyl, hydroxy, phenyl, cyano, amino, (C_1-C_6) -alkylamino, di- (C_1-C_6) alkylamino, $-C(=O)-NH-(C_1-C_6)$ alkyl, (C_1-C_6) alkyl- $C(=O)-NH-(C_1-C_6)$ alkyl, hydroxy (C_1-C_4) alkyl, (C_1-C_4) alkoxy (C_1-C_4) alkyl, $-NHC(=O)H$ and $-NHC(=O)-(C_1-C_6)$ alkyl; and

Q is a group of the formula



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m is an integer from 0 to 8, and any one of the carbon-carbon single bonds of $(CH_2)_m$ may optionally be replaced by a carbon-carbon double bond or a carbon-carbon triple bond, and any one of the carbon atoms of said $(CH_2)_m$ may optionally be substituted with R^{11} ;

R^6 is a radical selected from hydrogen, (C_1-C_6) straight or branched alkyl, (C_3-C_7) cycloalkyl wherein one of the carbon atoms may optionally be replaced by nitrogen, oxygen or sulfur; aryl selected from biphenyl, phenyl, indanyl and naphthyl; phenyl (C_2-C_6) alkyl, benzhydryl and benzyl, wherein each of said aryl and heteroaryl groups and the phenyl moieties of said benzyl, phenyl (C_2-C_6) alkyl and benzhydryl may optionally be substituted with one or more substituents independently selected from halo, nitro, (C_1-C_{10}) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_{10}) alkoxy optionally substituted with from one to three fluorine atoms, amino, hydroxy- (C_1-C_6) alkyl, (C_1-C_6) alkoxy- (C_1-C_6) alkyl, (C_1-C_6) -alkylamino, (C_1-C_6) alkyl-O- $C(=O)-$, (C_1-C_6) alkyl-O- $C(=O)-(C_1-C_6)$ alkyl, (C_1-C_6) alkyl- $C(=O)-O-$, (C_1-C_6) alkyl- $C(=O)-(C_1-C_6)$ alkyl-O, (C_1-C_6) alkyl- $C(=O)-$, (C_1-C_6) alkyl- $C(=O)-(C_1-C_6)$ alkyl-, di- (C_1-C_6) alkylamino, $-C(=O)NH-(C_1-C_6)$ alkyl, (C_1-C_6) -alkyl- $C(=O)-NH-(C_1-C_6)$ alkyl, $-NHC(=O)H$ and $-NHC(=O)-(C_1-C_6)$ alkyl; and wherein one of the phenyl moieties of said benzhydryl may optionally be replaced by naphthyl;

R^7 is hydrogen, phenyl or (C_1-C_6) alkyl;

or R⁶ and R⁷, together with the carbon to which they are attached, form a saturated carbocyclic ring having from 3 to 7 carbon atoms wherein one of said carbon atoms may optionally be replaced by oxygen, nitrogen or sulfur;

R⁸ and R⁹ are each independently selected from hydrogen, hydroxy, halo, amino, oxo (=O), nitrile, hydroxy-(C₁-C₆)-alkyl, (C₁-C₆)alkoxy-(C₁-C₆)alkyl, (C₁-C₆)alkylamino, di-(C₁-C₆)alkylamino, (C₁-C₆)alkoxy, (C₁-C₆)alkyl-O-C(=O)-, (C₁-C₆)alkyl-O-C(=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-C(=O)-O-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-O-, (C₁-C₆)alkyl-C(=O)-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-, and the radicals set forth in the definition of R⁶;

or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached;

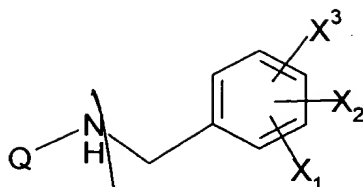
R¹⁰ is NHC(=O)R¹², NHCH₂R¹², NHSO₂R¹² or one of the radicals set forth in any of the definitions of R⁶, R⁸ and R⁹;

R¹¹ is oximino (=NOH) or one of the radicals set forth in any of the definitions of R⁶, R⁸ and R⁹; and

R¹² is (C₁-C₆)alkyl, hydrogen, phenyl(C₁-C₆)alkyl or phenyl optionally substituted with (C₁-C₆)alkyl;

with the proviso that (a) when m is 0, R¹¹ is absent, (b) neither R⁸, R⁹, R¹⁰ nor R¹¹ can form, together with the carbon to which it is attached, a ring with R⁷, (c) when R⁸ and R⁹ are attached to the same carbon atom, then either each of R⁸ and R⁹ is independently selected from hydrogen, fluoro, (C₁-C₆) alkyl, hydroxy-(C₁-C₆)alkyl and (C₁-C₆)alkoxy-(C₁-C₆)alkyl, or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached, (d) the nitrogen of formula I can not be double bonded to both Q and the substituted benzyl group to which it is attached, and (e) when neither X¹, X² nor X³ is a fluorinated alkoxy group, at least one of R⁶ and R⁷ is an aryl group substituted with a fluorinated alkoxy group, or a pharmaceutically acceptable salt thereof; effective in preventing or treating such condition, and a pharmaceutically acceptable carrier.

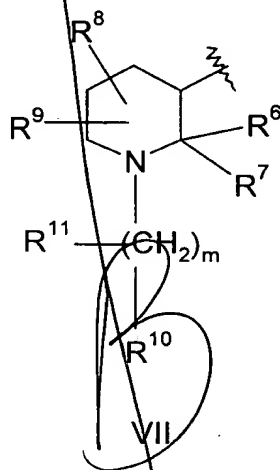
34. A pharmaceutical composition for antagonizing the effects of substance P in a mammal, comprising a substance P antagonizing effective amount of a compound according to the following formula



wherein X^1 is hydrogen (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms or (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms;

X^2 and X^3 are independently selected from halo, hydrogen, nitro, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms, trifluoromethyl, hydroxy, phenyl, cyano, amino, (C₁-C₆)-alkylamino, di-(C₁-C₆)alkylamino, -C(=O)-NH-(C₁-C₆)alkyl, (C₁-C₆)alkyl-C(=O)-NH-(C₁-C₆)alkyl, hydroxy(C₁-C₄)alkyl, (C₁-C₄)alkoxy(C₁-C₄)alkyl, -NHC(=O)H and -NHC(=O)-(C₁-C₆)alkyl; and

Q is a group of the formula



m is an integer from 0 to 8, and any one of the carbon-carbon single bonds of (CH₂)_m may optionally be replaced by a carbon-carbon double bond or a carbon-carbon triple bond, and any one of the carbon atoms of said (CH₂)_m may optionally be substituted with R¹¹;

R⁶ is a radical selected from hydrogen, (C₁-C₆) straight or branched alkyl, (C₃-C₇) cycloalkyl wherein one of the carbon atoms may optionally be replaced by nitrogen, oxygen or sulfur; aryl selected from biphenyl, phenyl, indanyl and naphthyl; phenyl (C₂-C₆) alkyl, benzhydryl and benzyl, wherein each of said aryl and heteroaryl groups and the phenyl moieties of said benzyl, phenyl (C₂-C₆) alkyl and benzhydryl may optionally be substituted with one or more substituents independently selected from halo, nitro, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms, amino, hydroxy-(C₁-C₆)alkyl, (C₁-C₆)alkoxy-(C₁-C₆)alkyl, (C₁-C₆)-alkylamino, (C₁-C₆)alkyl-O-C(=O)-, (C₁-C₆) alkyl-O-C(=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-C(=O)-

O-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-O, (C₁-C₆)alkyl-C(=O)-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-, di-(C₁-C₆)alkylamino-, C(=O)NH-(C₁-C₆)alkyl-, (C₁-C₆)-alkyl-C(=O)-NH-(C₁-C₆)alkyl-, -NHC(=O)H and -NHC(=O)-(C₁-C₆) alkyl; and wherein one of the phenyl moieties of said benzhydryl may optionally be replaced by naphthyl;

R⁷ is hydrogen, phenyl or (C₁-C₆)alkyl;

or R⁶ and R⁷, together with the carbon to which they are attached, form a saturated carbocyclic ring having from 3 to 7 carbon atoms wherein one of said carbon atoms may optionally be replaced by oxygen, nitrogen or sulfur;

R⁸ and R⁹ are each independently selected from hydrogen, hydroxy, halo, amino, oxo (=O), nitrile, hydroxy-(C₁-C₆)-alkyl, (C₁-C₆)alkoxy-(C₁-C₆)alkyl, (C₁-C₆)alkylamino, di-(C₁-C₆)alkylamino, (C₁-C₆)alkoxy-, (C₁-C₆)alkyl-O-C(=O)-, (C₁-C₆)alkyl-O-C(=O)-(C₁-C₆)alkyl-, (C₁-C₆)alkyl-C(=O)-O-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-O-, (C₁-C₆)alkyl-C(=O)-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-, and the radicals set forth in the definition of R⁶;

or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached;

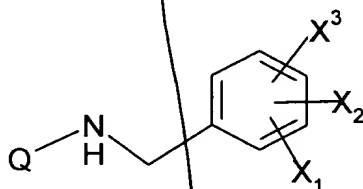
R¹⁰ is NHC(=O)R¹², NHCH₂R¹², NHSO₂R¹² or one of the radicals set forth in any of the definitions of R⁶, R⁸ and R⁹;

R¹¹ is oximino (=NOH) or one of the radicals set forth in any of the definitions of R⁶, R⁸ and R⁹; and

R¹² is (C₁-C₆)alkyl, hydrogen, phenyl, (C₁-C₆)alkyl or phenyl optionally substituted with (C₁-C₆)alkyl;

with the proviso that (a) when m is 0, R¹¹ is absent, (b) neither R⁸, R⁹, R¹⁰ nor R¹¹ can form, together with the carbon to which it is attached, a ring with R⁷, (c) when R⁸ and R⁹ are attached to the same carbon atom, then either each of R⁸ and R⁹ is independently selected from hydrogen, fluoro, (C₁-C₆) alkyl, hydroxy-(C₁-C₆)alkyl and (C₁-C₆)alkoxy-(C₁-C₆)alkyl, or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached, (d) the nitrogen of formula I can not be double bonded to both Q and the substituted benzyl group to which it is attached, and (e) when neither X¹, X² nor X³ is a fluorinated alkoxy group, at least one of R⁶ and R⁷ is an aryl group substituted with a fluorinated alkoxy group, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

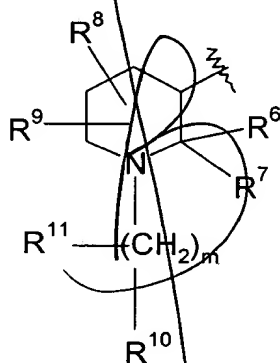
35. A pharmaceutical composition for treating or preventing a condition in a mammal, the treatment or prevention of which is effected or facilitated by a decrease in substance P mediated neurotransmission, comprising an amount of a compound according to the following formula,



wherein X^1 is hydrogen (C_1 - C_{10}) alkoxy optionally substituted with from one to three fluorine atoms or (C_1 - C_{10}) alkyl optionally substituted with from one to three fluorine atoms;

X^2 and X^3 are independently selected from halo, hydrogen, nitro, (C_1 - C_{10}) alkyl optionally substituted with from one to three fluorine atoms, (C_1 - C_{10}) alkoxy optionally substituted with from one to three fluorine atoms, trifluoromethyl, hydroxy, phenyl, cyano, amino, (C_1 - C_6)-alkylamino, di-(C_1 - C_6)alkylamino, $-C(=O)-NH-(C_1-C_6)alkyl$, (C_1-C_6)alkyl- $C(=O)-NH-(C_1-C_6)alkyl$, hydroxy(C_1-C_4)alkyl, (C_1-C_4)alkoxy(C_1-C_4)alkyl, $-NHC(=O)H$ and $-NHC(=O)-(C_1-C_6)alkyl$; and

Q is a group of the formula



m is an integer from 0 to 8, and any one of the carbon-carbon single bonds of $(CH_2)_m$ may optionally be replaced by a carbon-carbon double bond or a carbon-carbon triple bond, and any one of the carbon atoms of said $(CH_2)_m$ may optionally be substituted with R^{11} ;

R^6 is a radical selected from hydrogen, (C_1 - C_6) straight or branched alkyl, (C_3 - C_7) cycloalkyl wherein one of the carbon atoms may optionally be replaced by nitrogen, oxygen or sulfur; aryl selected from biphenyl, phenyl, indanyl and naphthyl; phenyl (C_2 - C_6) alkyl, benzhydryl and benzyl, wherein each of said aryl and heteroaryl groups and the phenyl moieties of said benzyl, phenyl (C_2 - C_6) alkyl and benzhydryl may optionally be substituted with one or

more substituents independently selected from halo, nitro, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms, amino, hydroxy-(C₁-C₆)alkyl, (C₁-C₆)alkoxy-(C₁-C₆)alkyl, (C₁-C₆)-alkylamino, (C₁-C₆)alkyl-O-C(=O)-, (C₁-C₆) alkyl-O-C(=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-C(=O)-O-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-O-, (C₁-C₆)alkyl-C(=O)-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-, di-(C₁-C₆)alkylamino-, C(=O)NH-(C₁-C₆)alkyl, (C₁-C₆)-alkyl-C(=O)-NH-(C₁-C₆)alkyl, -NHC(=O)H and -NHC(=O)-(C₁-C₆) alkyl; and wherein one of the phenyl moieties of said benzhydryl may optionally be replaced by naphthyl;

R⁷ is hydrogen, phenyl or (C₁-C₆)alkyl;

or R⁶ and R⁷, together with the carbon to which they are attached, form a saturated carbocyclic ring having from 3 to 7 carbon atoms wherein one of said carbon atoms may optionally be replaced by oxygen, nitrogen or sulfur;

R⁸ and R⁹ are each independently selected from hydrogen, hydroxy, halo, amino, oxo (=O), nitrile, hydroxy-(C₁-C₆)-alkyl, (C₁-C₆)alkoxy-(C₁-C₆)alkyl, (C₁-C₆)alkylamino, di-(C₁-C₆)alkylamino, (C₁-C₆)alkoxy, (C₁-C₆)alkyl-O-C(=O)-, (C₁-C₆)alkyl-O-C(=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-C(=O)-O-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-O-, (C₁-C₆)alkyl-C(=O)-, (C₁-C₆)alkyl-C(=O)-(C₁-C₆)alkyl-, and the radicals set forth in the definition of R⁶;

or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached;

R¹⁰ is NHC(=O)R¹², NHCH₂R¹², NHSO₂R¹² or one of the radicals set forth in any of the definitions of R⁶, R⁸ and R⁹;

R¹¹ is oximino (=NOH) or one of the radicals set forth in any of the definitions of R⁶, R⁸ and R⁹; and

R¹² is (C₁-C₆)alkyl, hydrogen, phenyl(C₁-C₆)alkyl or phenyl optionally substituted with (C₁-C₆)alkyl;

with the proviso that (a) when m is 0, R¹¹ is absent, (b) neither R⁸, R⁹, R¹⁰ nor R¹¹ can form, together with the carbon to which it is attached, a ring with R⁷, (c) when R⁸ and R⁹ are attached to the same carbon atom, then either each of R⁸ and R⁹ is independently selected from hydrogen, fluoro, (C₁-C₆) alkyl, hydroxy-(C₁-C₆)alkyl and (C₁-C₆)alkoxy-(C₁-C₆)alkyl, or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached, (d) the nitrogen of formula I can not be double bonded to both Q and the substituted benzyl group to which it is attached, and (e) when neither X¹, X² nor X³ is a fluorinated alkoxy group,

at least one of R⁶ and R⁷ is an aryl group substituted with a fluorinated alkoxy group, or a pharmaceutically acceptable salt thereof; ~~1B~~
effective in treating or preventing such condition and a pharmaceutically acceptable carrier.

36. A method for treating or preventing a condition selected from the group consisting of inflammatory diseases, anxiety, colitis, depression or dysthymic disorders, psychosis, pain, gastroesophageal reflux disease, allergies, chronic obstructive airways disease, hypersensitivity disorders, vasospastic diseases, fibrosing and collagen diseases, reflex sympathetic dystrophy, addiction disorders, stress related somatic disorders, peripheral neuropathy, neuralgia, neuropathological disorders, disorders related to immune enhancement or suppression, and rheumatic diseases in a mammal, comprising administering to a mammal in need of such treatment or prevention, an amount of a pharmaceutical composition according to claim 33 effective in preventing or treating such condition.

Sub B'
Q

37. A method for antagonizing the effects of substance P in a mammal, comprising administering to said mammal, a substance P antagonizing effective amount of a pharmaceutical composition according to claim 34.

38. A method for treating or preventing a condition in a mammal, the treatment or prevention of which is effected or facilitated by a decrease in substance P mediated neurotransmission, comprising administering to a mammal in need of such treatment or prevention an amount of a pharmaceutical composition according to claim 35 effective in treating or preventing such condition.

39. The method of claim 36, wherein for the compound of said pharmaceutical composition, X¹ is a 2-(C₁-C₄)alkoxy group, X² is hydrogen and X³ is a 5-OCF₃ or 5-OCHF₂ group.

40. The method of claim 36, wherein for the compound of said pharmaceutical composition, X¹ is a 2-OCF₃ or 2-OCHF₂ group, X² is hydrogen and X³ is (C₁-C₄) alkyl.

41. The method of claim 36, wherein for the compound of said pharmaceutical composition, R⁶ is present, is selected from phenyl optionally substituted with (C₁-C₄)alkyl. (C₁-C₄) alkoxy, fluorine, chlorine or trifluoromethoxy, each of R⁷, R⁸, R⁹ and R¹⁰ is hydrogen.

42. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-2-phenyl-3-[2-(2,2,2-trifluoroethoxy)-benzyl]aminopiperidine.

43. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine.

44. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-3-(2-hydroxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine.

45. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-2-phenyl-3-(3-trifluoromethoxybenzyl)aminopiperidine.

46. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-1-(5,6-dimethoxyhexyl)-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine.

47. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-2-phenyl-3-(2-trifluoromethoxybenzyl)aminopiperidine.

48. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-3-(5-chloro-2-(2,2,2-trifluoroethoxy)-benzylamino-2-phenylpiperidine.

49. The method of claim 36, wherein the compound of said pharmaceutical composition is (2S,3S)-3-(5-*t*-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine.

50. The method of claim 36, wherein the compound of said pharmaceutical composition is 3-(5-*tert*-butyl-2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)piperidine.

51. The method of claim 36, wherein the compound of said pharmaceutical composition is 3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenyl)piperidine.

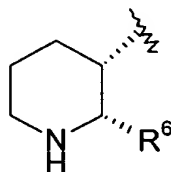
52. The method of claim 36, wherein the compound of said pharmaceutical composition is 3-(2-difluoromethoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine.

54. The method of claim 36, wherein for the compound of said pharmaceutical composition, X¹ is 5- trifluoromethoxy, X² is hydrogen and X³ is 2-methoxy.

55. The method of claim 36, wherein for the compound of said pharmaceutical composition, X¹ is 2-trifluoromethoxy and each of X² and X³ is hydrogen.

56. The method of claim 36, wherein for the compound of said pharmaceutical composition, X¹ is 2-(2,2,2-trifluoroethoxy) and each of X² and X³ is hydrogen.

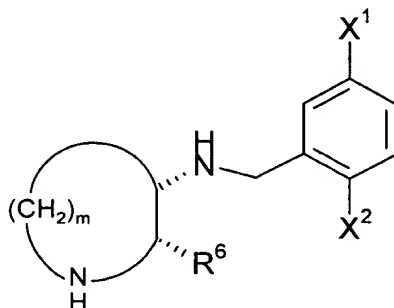
57. The method of claim 36, wherein for the compound of said pharmaceutical composition, Q is a group of the formula



wherein X¹ is 2-trifluoromethoxy,

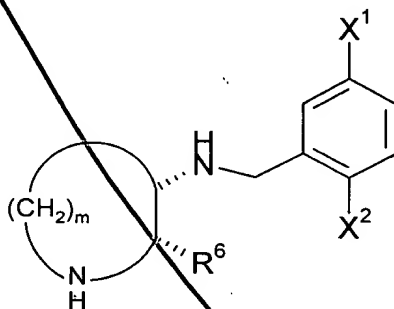
2-methoxy or 2-(2,2,2-trifluoroethoxy), X^2 is 5-halo, 5-(C_1 - C_6) alkyl, or 5-(C_1 - C_6) alkoxy optionally substituted with from one to three fluorine atoms, and $R_{sup.6}$ is substituted or unsubstituted phenyl.

58. The method of claim 36, wherein the compound of said pharmaceutical composition has the formula



wherein n is an integer from 2 to 4, X^1 is hydrogen or (C_1 - C_4)alkyl, X^2 is OCF_3 or $OCHF_2$, and R^6 is phenyl optionally substituted with a substituent selected from (C_1 - C_4)alkyl, (C_1 - C_4)l- C_4)alkoxy, fluorine and chlorine.

59. The method of claim 36, wherein the compound of said pharmaceutical composition has the formula



wherein n is, X^1 is OCF_3 or $OCHF_2$,

X^2 is (C_1 - C_4)alkoxy, and R^6 is phenyl optionally substituted with a substituent selected from (C_1 - C_4)alkyl, (C_1 - C_4)alkoxy, fluorine and chlorine.

60. The method of claim 36, wherein for the compound of said pharmaceutical composition, one or more atoms of such compound have been replaced with a radioactive isotope thereof.

61. The method of claim 60, wherein said compound contains one or more tritium or ^{14}C isotopes.

62. The method of claim 61, wherein for said compound R^6 is phenyl or substituted phenyl.